REMARKS/ARGUMENTS

Status of Claims

Claims 1-13 are pending and are under prosecution. Claims 1 and 13 are amended. Support is found in the clams as filed. Claim 8 is canceled. Claim 9 is amended in view of the cancellation of claim 8. Claim 10 is amended to correct a typographical error.

Information Disclosure Statement

The Examiner has acknowledged the Information Disclosure Statement submitted on December 19, 2007 and indicates it is being considered.

Claim Rejections Under 35 U.S.C. § 112

The rejection of claims 7 and 13 under 35 U.S.C. § 112, second paragraph, has been withdrawn. The rejection of Claims 1-13 and 13 under 35 U.S.C. § 112, first paragraph, has been withdrawn. Applicants appreciate the Examiner withdrawing the rejections.

Claim Rejections Under 35 U.S.C. § 103

Claims 1-3, 8-10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bechter et al. as evidenced by West et al. (US Patent No. 5,489,508). The Examiner cites Bechter as disclosing a method of predicting survival in patients with B cell chronic lymphocytic leukemia wherein the method includes determining the telomere length of human patients and correlating the telomeric length with mortality risk associated with B-CLL with telomere length in a population. The Examiner notes that Bechter do not predict the survival of a test patient based on their data and do not age-match the population to the patient being tested. Nonetheless, the Examiner suggests that the Bechter renders the cited claims obvious. Applicants respectfully traverse the rejection.

As argued previously, Bechter et al. correlates the median telomere length with survival of patients afflicted with B cell chronic lymphocytic leukemia (B-CLL). The median telomere length for these B-CLL patients was 6.0 kb. As shown in Figure 1, those B-CLL patients with a telomere length of less than 6.0 kb had a lower probability of survival as compared to those with a telomere length greater than 6.0 kb.

The claimed invention is distinguishable from Bechter in that Bechter discloses the correlation of the probability of survival as a function of telomere length for a diseased population. The claims are not directed to a correlation of an individual's telomere length with the telomere length of a diseased population. As indicated from the working example in the specification, the telomere length is compared the telomere length of a general population. As such, Bechter et al. does not anticipate or render obvious the claims.

Applicants also note that the Examiner has previously withdrawn the rejection of claims in view of Bechter. That is, as noted in the office action of May 12, 2008, the rejection was "withdrawn in view of a careful reconsideration". In addition, as set forth above, the Examiner noted that "Bechter...do not predict the survival of a test patient based on their data." "Bechter et al. do not age-match the population to the patient being tested." However, the Examiner has again rejected the claims based on this reference now in combination with West.

West, however, fails to cure the deficiency of Bechter. That is, the Examiner relies on West because "Tumour cells are also characterized by shortened telomeres..." (citing to col. 2, lines 26-27). However, this adds nothing to the teaching of Bechter that would render the instant claims unpatentable.

The Examiner also points to West for the teaching that "There are a number of possible mechanisms for loss of telomeric DNA during ag[i]ng..." (citing to col. 2, lines 36-37). However, this too fails to cure the deficiencies of Bechter. This provides nothing related to a method as claimed.

"There is a reduction in the length of telomere repeat arrays relative to the normal colonic mucosa from the same patient." (citing to col. 2, lines 57-58). This also fails to cure the deficiency of Bechter. This disclosure, which is related to a comparison

between cells *within the same patient*, provides no teaching or suggestion that renders the presently claimed method obvious when with Bechter.

"Telomere length has been found to be the best predictor of the remaining lifespan of cells cultured from donors of different ages. The ability to measure telomere length thus has significan [sic] clinical use." (citing to col. 29, lines 16-19). This too fails to render the present claims obvious. This teaching is related to telomeres of *cultured cells*, e.g. not cells from a patient as claimed. Also, this teaching is related to the lifespan of cultured cells, not mortality of a patient. Finally, Applicants note that this teaching is related to cells from donors of different ages, not age-matched.

The Examiner noted that one of skill in the art would have been motivated to "employ the art of using the telomeric length as a survival predictor for patients suffering from B-CLL." The Examiner cites to West for motivation to employ telomere length as an assay for cancer survival. However, we note that in both Bechter and West, telomere length from a patient is compared to telomere length from similarly afflicted subjects. That is, nowhere in Bechter or West is there disclosure of comparing telomere length from a subject to the telomere length of an age-matched but otherwise general population. Again, in both Bechter and West, telomere length was compared between cancer patients, or patients of *different ages*, for example. That is West repeatedly emphasizes that telomeres are shortened with increasing age of a subject. West teaches a comparison between different aged populations, not age-matched samples. Thus, the combination of cited references fails to teach a method in which telomere length from a subject is compared to telomere length of an age-matched population to correlate telomere length with mortality rate.

The Examiner stated that "one of ordinary skill in the art, at the time the invention was made would have been clearly motivated to employ the teachings of Bechter et al., that is, using the length of a telomere of a patient as a marker for predicting the survival of said patient, by comparing said telomere length to the average telomere length derived from a population *of patients*." (Emphasis added) However, we note the instant claims do not require comparison to a population *of patients*. Rather, a general population that is age-matched is used for comparison. Applicants submit that the

unexpected correlation between telomere length and mortality rate in an age-matched but otherwise general population provides evidence of unpredictability of the method as claimed.

In view of the above, we submit that the combination of references fails to disclose each of the limitations of the claims. Moreover, we find nothing in the combination of references that would have motivated one of skill in the art to practice or even attempt the claimed method. Finally, we submit that this art is highly unpredictable and that absent evidence of success in the identification of the correlation as claimed, one of skill in the art would not have a reasonable expectation of success in practicing the invention as claimed. As such, Applicants request the Examiner to withdraw the rejection.

Claims 1-3, 8-10, 12 and 13 are rejected under 35 U.S.C. 103 as being unpatentable over Chang et al. (PNAS, USA, 1995, vol. 92, pp. 11190-11194) as evidenced by West et al. (U.S. Patent No. 5,489,508).

According to the Examiner, Chang discloses that the length of telomeres is implicated with cardiovascular diseases. The Examiner noted that Chang et al. do not predict the survival of a test patient based on their data. Also, the Examiner noted that Chang et al. do not age-match the population to the patient being tested.

Nonetheless, the Examiner suggests that it would have been prima facie obvious to one of ordinary skill in the art to apply the teachings of Chang et al. for the purpose of predicting the survival of a patient who has had or is likely to have cardiovascular disease based on the length of the telomere. Applicants respectfully traverse.

The Examiner appears to rely on the statement in Chang et al. that "measurement of telomere length could be a useful procedure to detect alterations of cellular turnover in tissues associated with cardiovascular diseases" as motivation for one of skill in the art to practice the invention as claimed. (Citing Chang et al. p. 11193, first column, third full paragraph.) The Examiner cites to West for additional support for such motivation. We respectfully disagree.

As noted previously, Chang et al. analyzed telomere length from tissue samples from the aortic arch, abdominal aorta, iliac artery and iliac vein obtained from autopsies. Figure 3 discloses the mean telomere length as measured by telomere restriction fragments (TRF) for thoracic artery and iliac arteries as a function of donor age. Based on this and the other presented data, the authors conclude that the mean TRF length can serve as a marker for cell turnover of human vascular tissue and that it is possible that telomere length or other measures of cellular senescence could predict the functional status of tissues better than chronological age. See page 11193, column 2, paragraph 3.

The claims are distinguishable over Chang et al. because Chang et al. does not correlate the telomere length of a live individual with the somatic cell telomere length in a general population. Rather, the telomere length of a dead individual is compared with the telomere length of other dead individuals who have died of various causes. In addition, although Chang et al. assert that telomere length is a direct measure of proliferative history, it also acknowledges that to obtain telomere DNA one must obtain a biopsy of endothelial tissue which in itself can induce plaque formation thereby raising ethical and practical difficulties. See Chang 11193, column 2, paragraph 2. Notwithstanding Chang et al.'s assertion of an *in situ* assay for telomere length involving less than 100 cells, there is no disclosure that would facilitate such an assay. Accordingly, Chang et al. would not be applicable to determining the telomere length of endothelial tissue from a live individual.

Applicants note that the Examiner has previously withdrawn the rejection of claims in view of Chang. As noted in the office action of May 12, 2008, the rejection was "withdrawn in view of a careful reconsideration". In addition, as set forth above, the Examiner noted that "Chang...do not predict the survival of a test patient based on their data." "Chang et al. do not age-match the population to the patient being tested." However, the Examiner has again rejected the claims based on this reference now in combination with West.

West, however, fails to cure the deficiency of Chang. That is, the Examiner relies on West as described above for Bechter. Howevever, as noted above for Bechter, West fails to cure the deficiencies of Chang.

Moreover, while Chang does measure telomere length in different tissues, we find no disclosure in Chang teaching that telomere length in a subject was compared to telomere length of an age-matched population and correlated with mortality. Applicants find no teaching or suggestion in Chang of the method as claimed. As noted above, West fails to cure this deficiency. Thus, the combination of references fails to teach each limitation of the claims. Applicants respectfully request the Examiner to withdraw the rejection.

Claims 1-3 and 5-11 are rejected under 35 U.S.C. 103 as being unpatentable over Palmer et al. (The Journal of Experimental Medicine, 1997, vol. 185, no. 7, pages 1381-1386) as evidenced by West et al. (U.S. Patent 5,489,508).

According to the Examiner, Palmer discloses that the length of telomeres from CD8+ cells is correlated with HIV infected patients. However, the Examiner notes that Palmer do not predict survival of a test patient or age-match the population.

As noted previously, Palmer et al. disclose a method of correlating the decreased length of telomeres from $CD8^+$ T cells from HIV-infected patients. The Examiner acknowledges that Palmer et al. does not predict the survival of a test patient based on their data. The Examiner notes that Palmer do not age-match the population to the patient being tested. However, the Examiner asserts that Palmer et al. demonstrate the telomere length is decreased in patients infected with HIV and that decreased levels of T cells in humans is correlated with the progression of disease and the survival of patients inflicted with HIV.

However, the claims are patentable over Palmer et al. Palmer et al. uses cells derived from a diseased individual to determine telomere length in $CD8^+$ positive cells. Palmer et al. also compares telomere length with the telomere length of a monozygotic

twin rather than a general population. As such, the claims are patentable over Palmer et al.

Applicants also note that the Examiner has previously withdrawn the rejection of claims in view of Chang. As noted in the office action of May 12, 2008, the rejection was "withdrawn in view of a careful reconsideration". In addition, as set forth above, the Examiner noted that "Palmer...do not predict the survival of a test patient based on their data." "Palmer et al. do not age-match the population to the patient being tested." However, the Examiner has again rejected the claims based on this reference now in combination with West.

West, however, fails to cure the deficiency of Palmer. That is, the Examiner relies on West as described above for Bechter and Chang. However, as noted above for Bechter and Chang, West fails to cure the deficiencies of Palmer.

Moreover, while Palmer does measure telomere length in CD8+ cells we find no disclosure in Palmer teaching that telomere length in a subject was compared to telomere length of an age-matched population and correlated with mortality. Applicants find no teaching or suggestion in Palmer of the method as claimed. As noted above, West fails to cure this deficiency. Thus, the combination of references fails to teach each limitation of the claims. Applicants respectfully request the Examiner to withdraw the rejection.

Claim 4 is rejected under the 35 U.S.C. § 103a as beyond unpatentable over Bechter et al. and West in view of Kim et al. Bechter and West are applied as above and Kim is applied for its teaching of an amplification assay of telomerase product.

In addition, Claim 4 is rejected under 35 U.S.C. § 103 as being unpatentable over Chang et al. and West in view of Kim et al. Chang and West are applied as above and Kim is applied as above.

Likewise, Claim 4 is rejected under 35 U.S.C. § 103a as being unpatentable over Palmer et al. and West in view of Kim et al. Palmer and West are applied as above and Kim is applied as above.

Kim does not cure the deficiencies of Bechter et al. and West, Chang et al. and West and Palmer et al. and West as applied to Claim 1. Since Claim 1 is patentable over these references, Claim 4 is as well. Applicants request the Examiner to withdraw the rejection.

Conclusion

Applicants believe the present application is now in condition for allowance. An early and favorable communication thereof is therefore respectfully requested. If the Examiner believes that a telephone conference would expedite prosecution of the application, please call the undersigned at his direct line 415.442.1216.

Respectfully submitted,

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